Pharming Group N.V.
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PARTICIPANTS
Sijmen de Vries, MD – Chief Executive Officer
Anurag Relan, MD – Chief Medical Officer

Jeff Jones – Analyst (Oppenheimer):
Good morning, everyone, and welcome back to Oppenheimer's Day 2 of our 35th Annual Healthcare Conference. I am delighted to welcome the Pharming team with CEO, Sijmen de Vries kicking us off with a presentation and update on the story. Sijmen, I'll turn it over to you.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, Jeff. Good morning or good afternoon, ladies and gentlemen wherever you are. I'm pleased to give you the Pharming story today. And I'm here with my colleague Dr. Anurag Relan, our Chief Medical Officer who will take part of the presentation as well.

Before we do that, obviously, I have this slide with the forward-looking statements because we will be making some forward-looking statements in this presentation. As you know, actual results may differ significantly because these statements are based upon our current beliefs and plans.

So, without any further ado, I would like to take you through the Pharming story. And this is what we're here to do at Pharming. We're building a leading global rare disease biopharma company. And we do this because on the left-hand side you see there, we have our own RUCONEST® product from our own research, a recombinant C1 esterase inhibitor that is in the market in the U.S. since 2014 already for the treatment of acute attacks of hereditary angioedema.

And RUCONEST® is basically a recombinant protein replacement therapy. And despite it being so long on the market and despite many other targeted therapies that are on the market, this product continues to thrive as you can see here, continues to increase serving patients and more prescribers keep prescribing RUCONEST® and patients continue to be reliant on RUCONEST®, despite increased therapy options. And I will go to a little bit more depth in a couple of minutes.

And then with the cash flows that our RUCONEST® is generating because you can see here, RUCONEST® was delivering more than US$227 million in the first nine months of 2024 and against a very healthy gross margin. We have been able to first of all in-license Joenja® from Novartis back in 2019, a product that is actually serving, is the first and only disease modifying therapy for an ultra-rare disease called APDS, activated phosphoinositide 3 delta kinase syndrome, an ultra-rare immune deficiency. And my colleague Anurag will tell you a lot more about the underlying disease. and has been launched last year in the United States.

In fact, in the end of March it was approved and launched and we recorded for the first nine months of 2024, you can see here almost US$32 million in sales. And this product actually will be rolled out across the world. And you can see here a number of regulatory actions that are currently ongoing as well as the label, which is serving 12 years and upwards, pediatric patients and, very special for a company like us, the Japan clinical trials, because this product is also expected to bring us into Japan, the second biggest pharmaceutical market in the world.

And then on the right-hand side, you see the further development of our portfolio. At the moment we are engaged in acquiring a small public Swedish company Abliva with a lead compound KL1333 for the treatment of primary mitochondrial disease. And that transaction is of course continuing at this point in time and pending Abliva deal close, we expect to add this compound to our portfolio and Anurag again will give you some more details on the compound and the underlying disease.

And leniolisib also has opportunities to serve further patients in additional indications, primary immune deficiencies. And we have the second one that is currently in a Phase II dose finding study and the third indication we are waiting. We have received regulatory feedback and in the not-too-distant future will be announcing the start of another Phase II trial. So, in other words we're building up a portfolio here and a global reach for the company with the cash flows from RUCONEST® and of course Joenja® is expected to help the cash flows in the near future with that as well.

Total revenue guidance for last year was between US$280 million and US$295 million. And we will of course update you on the actual results in the beginning of March, I think the second week of March, when we present our full year results.

So, let's just quickly look at RUCONEST®, why it's such a unique product. As I was already saying, it's the only recombinant version of protein replacement therapy because that is the key problem in hereditary angioedema. The missing or non-functioning enzyme is C1 inhibitor. And that is basically what we provide these patients. Therefore, you see that RUCONEST® basically serves these patients that cannot get by on any of the other therapies that are available.

And the good news for all those hereditary angioedema patients over the last decade is that a number of prophylactic therapies have come in the market, including oral prophylactic therapies, but they all have one problem. They are so called targeted therapies, and they target the sort of central pathway, the bradykinin/kallikrein pathway, works in a lot of patients, but there is a remaining number of patients, about half of them under the prophylactic treatments, that still have breakthrough attacks. That is where RUCONEST® comes in.

Now, RUCONEST® is not a convenient product. The patients actually self-inject themselves IV, but it is very efficacious as you can see on this slide. And therefore, it is that RUCONEST® is typically used by these patients that either have breakthrough attacks on the prophylaxis or have failed on the most prescribed product, icatibant, which is a subcutaneous injection.

Now you can see here on this slide that RUCONEST® continues to serve the hereditary angioedema population because the fact is that these patients actually continue to need that efficacious treatment. And of course, we see that there's upcoming competition into the market, for instance, oral treatments for acute therapies, but they have the same issue. They're either tested in a

population that actually do respond to icatibant and that is actually precisely the population that RUCONEST® is not being used for, because RUCONEST® is used in patients that are resistant for icatibant. So therefore, we feel that RUCONEST® is pretty strongly positioned, also against the new competition and including the new oral compounds to come into the market.

And we therefore are very confident that RUCONEST® will continue to deliver the revenue level that we currently are enjoying from RUCONEST® and continue to generate the cash flows that actually will allow us to continue to invest to build our portfolio.

And then if we take a look at the opportunity for leniolisib, for Joenja®, you see here that we're going into an ultra-rare disease, also a new ultra-rare disease. So therefore, finding patients is the name of the game here. You see that we have an estimated 1.5 patients per million for the first indication APDS. We found almost, in the left-hand side of the slide you can see, half of those patients in the U.S. There of course are a number of those that are not yet eligible because they're under the age of 12. And if you then also see that we have already got, we reported more than 90, in fact 93 patients after the third quarter in 2024. You can see we're well on our way to get those patients on therapy.

And in addition to that, we're looking for more of those patients. We're looking for more of those patients by means of providing free genetic testing in the United States. And also elucidating the many Variants of Uncertain Significance, so called VUS that we find. And that is because of course, the disease is not fully described yet because it's new and there's a lot of patients that have mutations in the relevant gene but are not yet classified as pathogenic.

And Anurag will go a little bit further into that later on in the presentation, because that could actually bring a significant number of patients in addition to the ones that we have currently found. And therefore, we're very confident that we will be able to find those 500 or more patients in the United States that are suffering from APDS.

In the rest of the world, we found a greater number of patients already because often in countries outside of the United States, the healthcare systems are far more centralized and therefore those patients are already in the centers of excellence. However, there's still work to be done. As you can see there, we found in outside of the United States and about 640 patients already and we have 164 either on early access programs, paid named patient programs, or clinical studies. So there is a bolus of patients waiting for regulatory action outside of the United States that can be put on paid therapy in addition to those that are already on paid name patient programs outside of the United States.

And then of course, as I was alluding to earlier, we have a number of pediatric studies ongoing. And that will mean that in the not-too-distant future, the label will be expanded to the below 12s as well. And that means that both in the United States and outside of the United states, more than 25% of those patients of the total patient population that are not yet eligible will become eligible to treatment.

So that is basically the way we expect that the Joenja® franchise in APDS will be built up over the coming, let's say two to three years when we fully have rolled it out, both in a geographical sense

and have elucidated the patients that are suffering from APDS by means of fully describing the APDS indication when we have clarified the Variants of Uncertain Significance.

Then last but not least, this was already elucidated a little bit earlier. We have a Phase II proof of concept trial in the PID with immune dysregulation that is currently ongoing similar to APDS symptoms. And we have received regulatory feedback on the third indication. And you can see on the bottom there, it's also a primary immune deficiency, that this indication actually represents more than seven or almost five times the number of patients that could be eligible for treatment.

So, in other words, leniolisib is a franchise not only in APDS but also in other primary immune deficiencies and once executed on, will represent a far larger commercial opportunity towards the future than RUCONEST®.

And here is a visual depiction of what our pipeline currently looks like. As you can see here, of course, RUCONEST® and Joenja® are both marketed, and you see there they depicted both the pediatric label extensions and of course the geographic spread out that leniolisib will bring. And on the bottom, you see their KL1333 that's currently in the pivotal trial and where Anurag will talk a little bit more about.

So, with that said, I would like now to hand over to Anurag to talk to you through Joenja® and leniolisib for APDS and subsequent indications. Anurag over to you please.

Anurag Relan, MD – Chief Medical Officer:
Thanks, Sijmen. So yes, let's talk a little bit about Joenja® and APDS and some of the work that we're doing there as well as some of the things that we're studying in leniolisib outside of APDS. So, as you heard, Joenja® is a medication that's approved to treat patients with APDS that are 12 years of age and older and it's approved in the United States by FDA. APDS again is a syndrome that's caused by this hyperactivity in a pathway called the PI3K pathway. And that hyperactivity is specifically caused by mutations or variants in the genes that encode for this enzyme complex.

As a result of that hyperactivity, there's significant morbidity and mortality associated with this condition. And it's really important to also understand it's a genetic disease that has features that really begin early in childhood and become progressive over these patients' lives. Joenja® is an oral selective PI3Kδ inhibitor that modulates this pathway and helps to regulate that hyperactive signaling to normalize that pathway and eventually to normalize the phenotype in these patients.

The drug was approved in March of 2023 based on a randomized controlled clinical trial as well as an open label long-term extension study. It is again an oral product that can help modulate this pathway and correct the underlying immune defect. And importantly it helps regulate the immune deficiency as well as the immune dysregulation seen in these patients. And we'll talk a little bit about that because that's also really the launching point for where we think the leniolisib could be applied further outside of APDS. And again, we've seen a favorable safety profile in the long-term clinical studies as well as in the post marketing experience with Joenja®.

Next slide, please. So, one of the key things that you heard Sijmen talk about really with APDS is looking for patients. And again, the condition itself was only discovered about 10 years ago. So, there's a lot of medical education still needed to help immunologists and other physicians who see

these patients to help them recognize APDS in the appropriate patient type and then be able to of course share data on leniolisib to use it appropriately in those patients.

That of course includes using the typical methods of sharing medical information, including conferences and congresses. And we have a number of abstracts and publications both on APDS showing the progressive nature of the disease and the serious nature of the disease, as well as data on leniolisib, both from the clinical trials as well as data on APDS itself.

But one of the key aspects of looking for patients is really making that final diagnosis. And again, the diagnosis is made by a genetic test. That genetic test is widely available, and we also support further availability of that test through a sponsored no-cost testing program called navigateAPDS. We provide genetic counselors. We educate physicians and providers about genetic testing and how to identify APDS. That identification process also includes family testing. It's an autosomal dominant condition, so patients can inherit the condition.

So, it's important to also consider family members for testing and discussing whether they should be also potentially treated if found to have APDS. And again, this is also coordinated through a network of genetic testing, as well as genetic counseling that we provide to patients and their families.

One of the key things, however, that happens when you do large scale genetic testing is you start to see new variants, or what Sijmen already mentioned was called Variants of Uncertain Significance. These in essence are variants or mutations that have not been previously classified. So, the result is essentially inconclusive. And we have a number of ongoing research efforts that we are supporting through a number of academic institutions to help be able to elucidate what the actual variant is and whether it's disease causing or not.

And these activities are ongoing, and we expect in the near future to be able to talk more about these because there's, again, a large number of patients, more than 1,200 in the U.S. alone who had a genetic test done because they've had some symptoms of an immunological condition and then found to have a result that is a VUS, so an inconclusive result. And the work that we're supporting will help these patients eventually get a correct diagnosis so that the variant can be appropriately classified.

Next slide. And let's also talk about some of the other opportunities that we see with Joenja®. Of course, we have ongoing regulatory reviews because there's a large number of patients that we've seen outside of the U.S. too. You saw Sijmen mentioned those numbers where those patients are already diagnosed. So that in Europe, we have the CHMP review that is now expected, extended for us to be able to submit this single CMC request and that will be submitted in January of 2026.

The European regulators have already concluded positive clinical benefit and safety. So that was an important milestone during the review that's already been achieved. We also have already the UK marketing authorization that was provided last year and now we're in the last stages of evaluation by NICE, their reimbursement authority. There is a Japanese clinical study, which you heard Sijmen also mention where the enrollment is completed and we're expecting to be able to file for regulatory approval in mid of this year.

We have a number of expanded access and named patient programs because again, there's a large number of patients already diagnosed who need access and we're trying to help those patients by providing access in the appropriate manner. We also have a marketing authorization in Israel. There are submissions under review in Canada, Australia, and I think one of the key things that you heard me say earlier is that this is a genetic disease with features that begin early in childhood.

And as such, being able to intervene earlier in life and providing something that could potentially, as a disease modifying agent, really impact these patients more significantly is quite important. And we have already found across the world more than a quarter of the patients that we found who are below the age of 12. So, we have two studies that are ongoing in this population of younger patients with APDS.

The first study is already concluded, and we had some top line data shared at the end of last year and we'll be presenting at some academic conferences, medical conferences later this year. And we expect to be able to begin filing in the second half of this year with that data. There's also the second study that goes down even to an earlier age group, which is still a smaller group, however, again, thinking about the disease course significant for these patients.

Then I'll talk to you in the next slide a little bit about the possibilities that we see for leniolisib outside of APDS. Again, because there's a large number of patients who have a clinical phenotype, who have clinical features that look very similar to APDS, and we see a significant opportunity to be able to help these patients also.

So again, what we're doing here is looking at this broad group of what are called primary immunodeficiencies. And these are immune deficiencies that have a certain number of features. Largely, these features are immune dysfunction. Again, that's what defines them as an immune deficiency, but also there's a significant proportion of these patients who have what's called immune dysregulation. And in some ways, these are really two sides of the same coin, and because they have these features, they have actually a lot of features that look like patients that have APDS.

And APDS is one such example of a primary immunodeficiency with immune dysregulation. And so, what we've been doing is talking to immunologists who are working with APDS patients, and they come back and say, you know, there's a significant other population of patients who have 'APDS-like' features. But when we do the genetic testing, they come back negative for APDS. And so, on that basis and on the basis that we've seen in the literature and studies that have been performed that we've been part of, we've seen a group of patients that have this hyperactive signaling in that same pathway, but have other genetic deficiencies.

And so we've started a study at the NIH in this group. This is a significantly larger group already than APDS, about 7 per million. And this Phase II proof of concept study started in the fourth quarter of last year and is already enrolling patients in this study. We expect this study to complete later this year and then be able to provide data next year on next steps in this study.

On top of that, there's another primary immune deficiency indication that we're working on. We've already gotten regulatory feedback on this indication. This is on top of the 7 per million that we see

in the second indication, and we'll be announcing soon our plans here for how to develop this further. But in essence, all of these areas that we're looking at or both of these areas, diseases that we're looking at are patients that have an immune deficiency as well as clinical features that line up very much with APDS. So, we think the opportunity here is significant to be able to impact these patients.

Sijmen de Vries, MD – Chief Executive Officer:
Okay. So, let's now switch to Abliva, the proposed acquisition of Abliva. So, we did a public tender offer, and we launched that for SEK 0.45 in cash for each share of Abliva, totaling acquisition price of US$66 million. We are able to do that with our existing cash as you can see here on this slide. And we are also able to actually develop KL1333 from our future cash flows, from our building portfolio.

KL1333 was in-licensed by Abliva from Yungjin Pharm, a South Korean company. So, we are basically, we'll have to be paying single digits to low-double digit royalties plus some development and commercial milestones, which of course we will be very happy to pay in the future. The offer was declared unconditional and completed last week. In fact, we concluded that we had 87.7% of the shares tendered. We're looking for 90% of the shares and to actually to complete and basically start delisting the Abliva shares from the Stockholm Stock Exchange. And we therefore also extended the offer till the 20th of February in order to reach that 90% threshold.

And this is basically fully in line with the strategy of developing our high value pipeline because this is a compound that is in a pivotal trial for a rare disease that basically have very little, if anything, to offer for those patients.

And over to Anurag now to take you to the primary mitochondrial diseases and clinical trial for KL1333.

Anurag Relan, MD – Chief Medical Officer:
Thanks, Sijmen.

So again, we really see a significant opportunity here with KL1333. Just a little background, mitochondria, of course, are the powerhouses of cells that produce ATP, which is the necessary molecule that powers the entire body. Obviously, this is especially important in muscle cells, and we'll talk a little bit about that as that relates to the clinical trial design.

This is a genetic disease. It's a rare disease. There's a large number of patients already diagnosed with the condition. These patients, again, because of this the nature of their dysfunctional mitochondria suffer from severe fatigue and muscle weakness and unfortunately also reduced life expectancy. And they can't live a normal life because of these serious symptoms that they have.

KL1333 is a compound that directly targets the mitochondrial driven pathway that in these patients, with more than 30,000 patients already diagnosed in the U.S. and the EU5. There is a pivotal study ongoing with a positive interim futility analysis, and we'll talk a little bit about that. And the study is expected to read out in 2027 with potential FDA approval by the end of the following year. And really it leverages our existing platform to develop and commercialize rare disease products.

And let's talk a little bit on the next slide about the study design. Again, this is a study that was designed based on regulatory feedback. And we have feedback that both FDA and EMA have accepted the study as potentially as a registrational study. And furthermore, we have feedback that meeting one of the potential alternative primary endpoints could be sufficient for filing. And there's been an ongoing dialogue with FDA to facilitate the study design and in fact, the entire development program.

The study design is a double-blind placebo controlled parallel group study with a three to two randomization favoring active drug over placebo. These are patients with mitochondrial DNA mutations as well as clinical features of the fatigue and myopathy that we talked about. And then the endpoints are based on fatigue as well as trying to assess their muscle weakness. After completion of the randomized part of the study, the patients will roll over into an open label extension study.

And on the next slide, we can talk a little bit about what that study looks like. Again, the study has been conducted – it will be conducted in two parts. The first part Wave 1 already has fully enrolled with 40 patients across 18 sites in six countries. There was an interim analysis conducted at when these 40 patients completed their 24 weeks. And that interim analysis specifically showed that both primary endpoints passed futility.

And this was an important aspect in terms of this development program because this allows us to give us some more confidence and really de-risk the program by showing that that if these trends continue, this could be a successful study at the completion of the trial. Also, important as part of this review, the data monitoring committee saw a favorable safety and tolerability profile and the study design was increased to 180 total patients to have the appropriate power.

We expect now after completion and acquisition of the deal that we'll be able to expand the study to the 180 patients who will be treated for 48 weeks. And these are existing sites that Abliva have opened. So, we expect that to be able to resume enrolling patients quickly as well as opening new sites to be able to accelerate the development of the plan.

And so again, it really builds on this platform that we built in terms of our rare disease expertise to be able to develop and commercialize. It will be incredibly important for this group of patients because it will be the first therapy really targeting this pathway. And again, there's a large number of patients already diagnosed. These are concentrated at several centers of excellence. There's number of patient advocacy groups that are also very active. And again, it's a small molecule tablet with low cost of goods and of course it's orally administered.

And with that, I'll turn it back to you Sijmen to talk about financials and wrap it up.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you, Anurag. Thank you very much.

Yeah, briefly the financials, this looks at the third quarter results. And you see a healthy comparison in terms of the sales growth versus 2023. Also, you see gross profit growing in line. You also see though OpEx, of course, growing as well. That had to do, of course, with investments that we had to do in marketing and sales, but also investments in R&D, and an increasing G&A expense because

of the expansion of the company. And of course, lots of rules and regulations that surround a company like ours with the dual listing.

But nevertheless, you could see that quarter three turned a very nice profit. And important as well as you can see here, we started generating cash again and that actually pays to what we said. That's an important thing to keep taking a good look at for the future because this is actually the fact why we took the decision to acquire Abliva from our own existing cash resources, the acquisition price of US$66 million and also because of the fact that we expect to continue to generate cash so that we can actually absorb the development costs of KL1333 from our own means.

And by the way, this is the last slide here, the guidance for 2024. I talked about the numbers before, and we will report those in the second week of March. But another important takeaway here is that we will not stop here, of course. We are building a portfolio, and we are continuing to look for acquisitions or preferably in-licensing of those clinical stage compounds, and Abliva is a very good case in point where we see that a compound is either in pivotal trial or later in development and represents an interesting opportunity for us to further leverage our commercialization and our development skill sets and, of course, rollout globally because we're putting a global footprint in place over the coming years. So that is how we are building a global rare disease company over the coming years.

And I think we're coming to the end of our time, so we can move forward.

Jeff Jones – Analyst (Oppenheimer):
Yeah. We're a touch over, Sijmen. So unfortunately, we won't have time for questions. But thank you very much for the presentation and the great update on the story. Obviously, looking forward to the 4Q results in a couple of weeks and the closing of the transaction. So good luck with everything. Have a great set of one-on-one meetings and look forward to catching up again soon.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, Jeff. Thank you.

Anurag Relan, MD – Chief Medical Officer:
Thank you.

Jeff Jones – Analyst (Oppenheimer):
All right. Take care, guys.

[END OF TRANSCRIPT]